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10/518,043	12/16/2004	Shinya Nagashima	Q85356	7583

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EXAMINER	
RAO, DEEPAK R	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,043	NAGASHIMA ET AL.	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *6* is/are allowed.

6)☒ Claim(s) *1-5, 7-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20050310 & 20070412*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-14 are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition as a therapeutic agent for asthma; or a method for treating asthma, does not reasonably provide enablement for a composition as a therapeutic or preventive agent generally; or a method for inhibitory activity of STAT 6 activation or Th2 cell differentiation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The instant claims 8-10 are drawn to 'a composition which is a **preventive** or therapeutic agent'. When a compound or composition claim is limited by a particular use, enablement of that claim should be evaluated based on that limitation. See MPEP § 2164.01(c). In contrast, when a compound or composition claim is **not** limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for non-enablement based on how to use.

The instant claims 8-10 are drawn to 'a composition which is a preventive or therapeutic agent'; claims 11-12 are drawn to 'use of the compound for the manufacture of STAT 6 activation inhibitor or Th2 cell differentiation inhibitor'; and claims 13-14 are drawn to 'a method of inhibitory activity for STAT 6 activation or Th2 cell differentiation'. According to the specification (see page 45), these agents and the activity recited are useful in treating respiratory diseases and allergic diseases. The instant claims, however, appear to be 'reach through' claims. Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through any or all diseases, disorders or conditions, for which they lack written description and enabling disclosure in the specification thereby requiring undue experimentation for one of skill in the art to practice the invention.

The testing assays provided in the specification in Examples 259-271 are related to measuring the STAT 6-dependent reporter; or Th2 differentiation activity of the compounds, however, there is nothing in the disclosure regarding how this data correlates to the **preventive** and therapeutic agents recited in the instant claims which may be used to a wide variety of therapeutic and/or preventive treatments. The diseases and disorders encompassed by the instant claims include respiratory diseases, allergic diseases, etc., some of which have been proven to be

extremely difficult even to treat and the instant claims recite the use as a **preventive drug**. Further, there is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. Note *In re Surrey*, 151 USPQ 724 regarding sufficiency of disclosure for a Markush group.

The number and complexity of allergenic triggers rise with each year that passes, the incidence of allergic diseases rises, and diseases like eczema have now reached epidemic proportions with no end in sight. Doctors and researchers struggle to find an effective therapeutic remedy, but so far have achieved only palliative remedies. Allergic reactions or diseases may involve any part of the body; the most frequently involved are the nose and chest with resultant symptoms of hay fever, rhinitis or asthma, respectively. The skin and eyes also commonly show allergic symptoms. Anaphylactic shock is a severe allergy, which affects many organs at the same time causing a rapid decrease in blood pressure, fainting and, occasionally, death. Allergies come in a variety of forms and vary in severity from mildly bothersome to life threatening and there is no single method of treatment, which is known to be effective against all types of allergies.

Further, the instant claims 8-10 recite that 'the composition is a **preventive agent** for respiratory diseases, asthma and chronic obstructive pulmonary disease, and there is no disclosure regarding how all these types diseases are **prevented**. See MPEP § 2164.03 for enablement requirements in cases directed to structure-specific arts such as the pharmaceutical art. The specification or the state of the art, however, does not provide any support for the **preventive** treatment of the types of diseases of the instant claims.

There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) claimed herein and therefore, require the treatment. Next, applicant's attention is drawn to the Revised Utility and Written Description Guidelines, at 66 FR 1092-1099, 2001 wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed 'oral preventive drug' solely based on the provided test data disclosed for some of the invention compounds.

The diagnosis of each of the disease is generally suggested by medical history and reports of endoscopy, cytology, X-ray, biopsy, etc. depending on the symptoms, signs and complications, which is essential to establish the dosage regimen for appropriate treatment or prevention. The disclosure does not provide any guidance towards the dosage regimen required to facilitate the treatment and/or inhibition of the claimed disorders, nor indicate competent technical references in the appropriate methods.

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(Only a few of the claimed diseases are discussed here to make the point of an insufficient disclosure, it does not definitely mean that the other diseases meet the enablement requirements).

Furthermore, the scope of the claims is not adequately enabled solely based on the antimicrobial activity provided in the specification. The instant claims are drawn in part to a **preventive agent**, which is not remotely enabled. "To prevent" actually means *to anticipate* or *counter in advance, to keep from happening etc.* (as per Websters II Dictionary) and therefore it is not understood how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "preventive" effect. There is no evidence of record that would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease or disorder claimed herein.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 and 7-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1. The preamble of claim 1 is confusing. The claim recites "A STAT 6 activation inhibitor" which appears to be drawn to 'a compound', however, as the claim contains the open ended recitation of "comprises" and from the recitation of 'a pharmaceutically acceptable carrier', it appears that claim 1 is intended to be 'a composition' claim. If composition is intended, changing the preamble appropriately to recite -- A composition -- is suggested.
2. Claim 2 merely recites a characteristic of the composition of claim 1 and does not further limit claim 1.
3. In claim 1, in line 2, the term " **derivative** " is indefinite. The term does not set forth the metes and bounds of the compounds intended by the claim. The term "**derivative**" may be interpreted as a residue derived from the compounds or a modification to the compounds recited in the claims, and it is confusing which compounds are derived from or modified to, from the other ingredients or compounds recited in the claims. The term is present in claims 3-5, 7 and 11-14.
4. Claims 8-10 merely recites an intended use for the composition of claim 7 and does not further limit claim 7.
5. Claim 11 recites the limitation "use of a diaminopyrimidnecarboxamide derivative represented by the general formula (I) described in claim 1" in lines 1-2, and therefore, the claim is drawn to the 'use of a compound of formula (I)'. Claim 1, however, is drawn to 'a composition which comprises the compound of formula (I)' and not the compound of formula (I) and therefore, claim 11 does not properly refer to the base claim. The discrepancy is present in claims 12-14 as well.

6. Claims 11-12 provide for the use of the compound, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 101

Claims 11-12 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Claims 1-2 and 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Taylor et al., CAPLUS Abstract 55:33107 (1961). The instantly claimed composition reads on reference disclosed composition. The reference teaches 4-amino-2-anilino-5-

pyrimidinecarboxamide compound (see RN 99844-93-6) in the presence of water. The preamble 'STAT 6 activation inhibitor' is not given patentable weight.

2. Claims 1-2 and 11-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Hisamichi et al., WO 99/31073 (cited in IDS). (U.S. Patent No. 6,432,963 which belongs to the same patent family, also cited in IDS, is reviewed as the WO publication is not in English). The instantly claimed composition reads on reference disclosed composition. See the reference disclosed compounds of Examples 8 and 52 of Table 5. The reference teaches a pharmaceutical composition comprising the compound and a pharmaceutically acceptable carrier, see col. 15. The preamble 'STAT 6 activation inhibitor' is not given patentable weight. Further, the instant claims 13-14 recite 'a method for inhibitory activity of STAT 6 activation in a mammal' and 'a method for inhibitory activity for Th2 cell differentiation in a mammal' using a compound of formula (I) and the specification provides that the compounds are useful in the treatment of respiratory diseases such as asthma, see page 45. The reference compounds are also disclosed to be useful as pharmaceutical therapeutic agents for the treatment of asthma, etc., see col. 13, lines 20-38. The reference and the instant claims recite administration of the compounds to the same patient population in same dosages for the same or analogous therapeutic utility.
3. Claims 1-2 and 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Bradbury et al., WO 00/39101 (cited in IDS). The instantly claimed composition reads on reference disclosed composition. See the reference disclosed compound of Example 7 (page 57). The reference teaches a pharmaceutical composition comprising the

compound and a pharmaceutically acceptable carrier, see page 50, lines 20-23. The preamble 'STAT 6 activation inhibitor' is not given patentable weight.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 5 and 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hisamichi et al., WO 99/31073. The reference teaches a generic group of pyrimidine-5-carboxamide compounds, which embraces applicant's instantly claimed compounds. See formula (I) in col. 3, and compound 52 of Table 5. The compounds are taught to be useful as pharmaceutical therapeutic agents for the treatment of asthma, etc., see col. 13, lines 20-38. The instant claims differ from the reference by reciting specific species or a more limited subgenus than the reference. For example, the instant claim differs by having a 3-chloro substituent on the

4-OH-phenyl ring as compared to compound 52 of the reference. The reference, however, teaches the equivalency of compounds wherein the aryl group substituted by 1 to 4 substituents. It would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the species of the genus taught by the reference, including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as taught for the genus as a whole i.e., as therapeutic agents. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus. *In re Susi*, 440 F.2d 442, 169 USPQ 423, 425 (CCPA 1971), followed by the Federal Circuit in *Merck & Co. v. Biocraft Laboratories*, 847 F.2d 804, 10 USPQ 2d 1843, 1846 (Fed. Cir. 1989).

Duplicate Claims

1. Applicant is advised that should claim 1 be found allowable, claim 2 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 2 merely recites another characteristic for the composition of claim 1, but does not further limit the claim.

2. Applicant is advised that should claim 7 be found allowable, claims 8-10 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two or more claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claims 8-10 merely recite an intended use for the composition of claim 7, but does not further limit the claim.

Allowable Subject Matter

Claim 6 is allowed. The references of record do not teach or fairly suggest the instantly claimed compounds.

Receipt is acknowledged of the Information Disclosure Statements filed on March 10, 2005 and April 12, 2007 and copies are enclosed herewith.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Monday-Friday from 8:00am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Deepak Rao/
Primary Examiner
Art Unit 1624

September 21, 2007